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EXAMINER

ODELL, LINDSAY T

ART UNIT	PAPER NUMBER
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1656

DATE MAILED: 07/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/733,776

Applicant(s)

RIEPING, MECHTHILD

Examiner

Lindsay Odell

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 April 2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 11-27 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 11-27 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 12 December 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>18 November 2004</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Application Status

1. In response to the previous Office action, a written restriction requirement (mailed on February 25, 2005), Applicants filed a response received and amendment on April 21, 2005. New claims 11-27 are added and original claims 1-10 are cancelled by virtue of the instant amendment. Claims 11-27 are pending in this instant Office action.

Election of Species

2. Applicant's election, without traverse, of the species *tdh* in claim 18 in the reply filed on April 21, 2005 is acknowledged. The requirement is, therefore, made FINAL. Inspection of the prior art revealed that it was not burdensome to search additional species. Thus, examination has been extended to include all of the species included in claims 17 and 18. Claims 11-27 are pending in the instant Office action. Claims 11-27 are examined herein.

Priority

3. The instant application is granted the benefit of priority for the foreign application 103 03 571.0 filed in Germany on January 30, 2003 as requested in the declaration. Receipt is acknowledged of papers submitted under 35 U.S.C. § 119(a)-(d) or (f), which papers have been placed of record in the file. Examiner notes that said papers are not in English and no translation has been filed.

Information Disclosure Statement

4. The information disclosure statements filed on November 18, 2004 has been reviewed, and its references have been considered as shown by the Examiner's initials next to each citation on the attached copy.

The Examiner notes that the Abstracts listed in references C71-C74 have been considered; however, they are crossed out because they refer to documents previously listed in the IDS and they will not be published on the front of the file. A copy of the document listed in C74 is actually an abstract of WO 20030806 A2, which claims priority to DE 101 35 053; thus, an English translation of the abstract of DE 101 35 053 has not been provided.

Compliance with Sequence Rules

5. The sequence listing, filed in computer readable form (CRF) and paper copy on December 12, 2003, has been received and entered.

Objections to the Specification

6. The specification is objected to because the title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: ---Processes for the fermentative preparation of L-threonine using strains of *Escherichia* in which the *yjgF* gene is inactivated---.

7. The specification is objected to for being improperly arranged. The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

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Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

- (a) TITLE OF THE INVENTION.
- (b) CROSS-REFERENCE TO RELATED APPLICATIONS.
- (c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
- (d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT
- (e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC (See 37 CFR 1.52(e)(5) and MPEP 608.05. Computer program listings (37 CFR 1.96(c)), "Sequence Listings" (37 CFR 1.821(c)), and tables having more than 50 pages of text are permitted to be submitted on compact discs.) or
REFERENCE TO A "MICROFICHE APPENDIX" (See MPEP § 608.05(a). "Microfiche Appendices" were accepted by the Office until March 1, 2001.)
- (f) BACKGROUND OF THE INVENTION.
 - (1) Field of the Invention.
 - (2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
- (g) BRIEF SUMMARY OF THE INVENTION.
- (h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
- (i) DETAILED DESCRIPTION OF THE INVENTION.
- (j) CLAIM OR CLAIMS (commencing on a separate sheet).
- (k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
- (l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

In particular, the Brief Description of the Drawings is improperly placed after the

Detailed Description of the Invention, instead of before it. Appropriate correction is required.

Claim Objections

8. Claim 17 is objected to because of the following informalities:

a) A single gene is listed in each of parts a)-eee), except for part g), which contains two genes: *pntA* and *pntB*. Although *pntA* and *pntB* encode subunits of a single protein, they are distinct genes and should be listed separately (i.e. in parts g) and h)) or the language --a gene selected from *pntA* and *pntB* . . . --- should be used.

b) In parts y), z), yy) and zz), gene names that begin with the letter 'a' are preceded by the article 'a', instead of ---an--- (i.e. "a *ahpC* gene", instead of ---an *ahpC* gene---). Words that begin with "a" must be preceded by the article ---an--- or another article besides "a".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 11-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "**modified**" in the phrase "modified enterobacterium" in claims 11, 17 and 18 is unclear as to the metes and bounds it imparts on the claimed subject matter. It is unclear what constitutes a "modified" enterobacterium. Does Applicant mean to claim enterobacteria of the genus *Escherichia* that have been modified by having their *yjgF* gene inactivated, or enterobacteria that are modified in a particular way and which also have their *yjgF* gene inactivated? If Applicant means to claim the latter, it is unclear what changes constitute

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modifications of the enterobacteria. For example, is an enterobacteria modified by virtue of having been selected for a particular resistance to antimetabolites or amino acids, as taught on pages 1 and 5-6 of the specification; having enhanced known threonine biosynthesis enzymes, as taught on page 13 of the specification; or must it have been transformed with DNA as taught on pages 23-26 of the specification? Clarification is required.

10. Claims 11 and 14-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "the *yjgF* open reading frame" of a modified enterobacterium of the genus *Escherichia* in claims 11, 20 and 21 is unclear. First, the exact nature of a *yjgF* open reading frame is unclear since the sequence for only one *yjgF* ORF from *Escherichia* is disclosed in the specification (*Escherichia coli yjgF*, SEQ ID NO: 1, see page 6), and several ORFs are known in the art in *Escherichia coli* that can be considered *yjgF* ORFs, but which have different names (i.e. *yhaR*, and *fl28*, Volz et. al, Figure 1, see IDS). Does *any* gene the encodes a YjgF protein meet the limitations of the claim or only genes that are exactly names "*yjgF*"? If *any* gene that encodes a YjgF protein meets the limitations of the claims, what exactly is a YjgF protein? Clarification is required.

11. Claims 17 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear exactly which genes must be over-expressed or inactivated in the instant claims. For example, consider the phrase "a *mgo* gene coding for malate:quinone

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oxidoreductase". If *E. coli* is the microorganism, must the *E. coli* mqo gene be over-expressed in the process for producing an L-amino acid, or can *any* mqo gene (from any organism) be over-expressed? In addition, if a malate:quinone oxidoreductase gene was named ---gene A--- (and not mqo) would its use read on the instant claims? Clarification is required.

12. Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "a *thrA* gene coding for aspartate kinase / homoserine dehydrogenase I" is confusing. Aspartate kinase and homoserine dehydrogenase are enzymes that have very different activities. Does Applicant mean to claim the *thrA* gene, which codes for both aspartate kinase *and* homoserine dehydrogenase I, instead or for a protein that is either aspartate kinase *or* homoserine dehydrogenase I? Clarification is required.

13. Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrases "a *pntA* and a *pntB* gene coding for the subunits of pyridine transhydrogenase, "a *ahpC* gene encoding the small subunit of alkyl hydroperoxide reductase" and "a *ahpF* gene encoding the large subunit of alkyl hydroperoxide reductase" are unclear as to the metes and bounds they impart on the claimed subject matter. It is unclear how many subunits pyridine transhydrogenase has, how they are defined, and which ones are encoded by *pntA* and *pntB*, respectively. Likewise it is unclear how many subunits alkyl hydroperoxide reductase has, and which subunits constitute the "small" and "large" subunits. Clarification is required.

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14. Claim 24 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "maximum amount" is unclear as to the metes and bounds of the claimed subject matter. It is unclear how to tell when the "maximum" amount of a given L-amino acid has been formed during fermentation. Is it after a certain number of hours of fermentation under certain conditions, or when L-amino acids in the broth reach a certain concentration? It is unclear how to measure when the "maximum amount" of any L-amino acid formation has been reached. Clarification is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 11, and 14-27 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 11 is drawn to processes using modified *Escherichia* wherein the *yjgF* open reading frame (ORF) of said modified *Escherichia* bacteria is claimed solely by name and without any functional limitations and insufficient structural limitations.

The Court of Appeals for the Federal Circuit has recently held that a “written description of an invention involving a chemical genus, like a description of a chemical species, ‘requires a precise definition, such as be structure, formula [or] chemical name,’ of the claimed subject matter sufficient to distinguish it from other materials.” *University of California v. Eli Lilly and Co.*, 1997 U.S. App. LEXIS 18221, at *23, quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these (*Enzo Biochem* 63 USPQ2d 1609 (CAFC 2002)).

University of Rochester v. G.D. Searle & Co. (69 USPQ2d 1886 (2004)) specifically points to the applicability of both *Lily* and *Enzo Biochemical* to methods of using products, wherein said products lack adequate written description. While in *University of Rochester v. G.D. Searle & Co.* the methods were held to lack written description because not a single example of the product used in the claimed methods was described, the same analysis applies wherein the product, used in the claimed methods, must have adequate written description as noted from *Enzo Biochemical* (see above).

On pages 6-7 of the instant specification, a *yjgF* ORF is disclosed that has a structure described by SEQ ID NO: 1 (and encoding SEQ ID NO: 2). The only known function for SEQ

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ID NO: 1 is to enhance L-threonine biosynthesis when it is inactivated. Applicants have described structural features of the genus relating to SEQ ID NO: 1 (and encoding SEQ ID NO: 2); however, a functional limitation is lacking, and the structural limitation that the instant gene be obtainable using primers SEQ ID NO: 3 and SEQ ID NO: 6 is insufficient because the primers only describe a small portion of an *yjgF* ORF. In addition, a representative number of species of *Escherichia yjgF* ORF's are not disclosed or found in the art, nor are the common structural characteristics of species in the instant genus that correlate to a functional limitation described. In view of the prior art, one of skill in the art would be unable to predict the structure of other members of this genus by virtue of the instant disclosure. Therefore, claims drawn to processes using the instant genus of *yjgF* ORFs are not adequately described.

16. Claims 17-18 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 17 and 18 are drawn to processes using *Escherichia* in which certain genes are overexpressed (claim 17) or inactivated (claim 18) wherein the gene is claimed solely by name and without any structural limitations; the specific genes are as follows: (1) protein imparting homoserine resistance, (2) protein imparting threonine resistance, (3) threonine export carrier protein, (4) DNA-binding protein HLP-II, (5) enzyme I of the phosphotransferase system, (6) glucose-specific IIA component, (7) glucose-specific IIBC component, (8) regulator of the leucine regulon, (9) Csr (10) regulator of the fad regulon, (11) regulator of the central intermediate metabolism, (12) 10 Kd chaperone, (13)

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regulator of the *cys* regulon, (14) PhoB, (15) sensor protein of the *pho* regulon, (16) protein E, (17) periplasmic binding protein of maltose transport, (18) protein with anti-sigmaE activity, (19) global regulator of the sigmaE factor, (20) periplasmic protein with a chaperonin-like function, (21) periplasmic protein with a chaperonin-like function, (22) periplasmic galactose-binding transport protein, (23) iron storage homoprotein, (24) regulator of sigmaE factor activity, (25) *yifA*, (26) *yifP*, (27) DgsA, (28) fructose repressor and (29) sigma³⁸ factor. While the function and structure of species of said genera of genes are disclosed in the specification, the structure of each species is not adequately described, nor are the common functional or structural characteristics of species that describe said genera identified.

The Court of Appeals for the Federal Circuit has recently held that a “written description of an invention involving a chemical genus, like a description of a chemical species, ‘requires a precise definition, such as be structure, formula [or] chemical name,’ of the claimed subject matter sufficient to distinguish it from other materials.” *University of California v. Eli Lilly and Co.*, 1997 U.S. App. LEXIS 18221, at *23, quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these (*Enzo Biochem* 63 USPQ2d 1609 (CAFC 2002)).

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Unlike genes such as *gdh* encoding glutamate dehydrogenase, the instant genes encode enzymes that do not have well known structures associated with them in the art. The instant specification describes one or two examples of each on pages 14-19. In the claims, these genes are only described according to the functional characteristics (or name) of the enzymes they encode; no structural relationship is described or used. Thus, one of skill in the art would be unable to predict the structure of other members of this genus by virtue of the instant disclosure. Therefore, claims drawn to methods using *Escherichia* in which these genes are overexpressed or inactivated are not adequately described.

17. Claims 11 and 14-27 are rejected under 35 U.S.C. 112, first paragraph, scope of enablement, because the specification, while being enabling for processes using *Escherichia coli* having an inactivated *yjgF* ORF described by SEQ ID NO: 1 in which certain genes are additionally over-expressed or inactivated, does not reasonably provide enablement for deleting the *yjgF* ORF in any species of *Escherichia* (claims 11, 14-18, 20-27), deleting any *yjgF* ORF in *E. coli* (claim 19), for producing any L-amino acid (claims 11, 14, 16-27), and for additionally expressing or attenuating all of the genes listed in claims 17-18. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. To produce the products necessary to practice the claimed methods would require undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized in *re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988). The Court in *Wands* states: "Enablement is not precluded by the necessity for some experimentation such as

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routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404).

Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

On page 6, the specification describes one gene within the genus of *Escherichia yjgF* ORFs: *E. coli yjgF* ORF described by SEQ ID NO: 1 (and encoding SEQ ID NO: 2). The only disclosed function of SEQ ID NO: 1 is that when inactivated it increases production of L-amino acids in *E. coli*, in particular, L-threonine (see page 27). On pages 23-27, the specification discloses the use of *E. coli* in which SEQ ID NO: 1 is inactivated for the production of L-threonine. Thus, one working example of *Escherichia* in which a *yjgF* ORF is inactivated for producing L-amino acids is provided.

Applicants, however, present no guidance or working examples of the use of any other *Escherichia yjgF* ORF for producing any other L-amino acid. The state of the prior art is such that few *yjgF* ORF's in the *Escherichia* genera (for example in *E. alberti*, *E. battae*, *E.*

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fergusonii) are known. The only other *yjgF* ORF's known in the art are *E. coli yhaR* and *fl28* (Figure 1, Volz *et al.*, see IDS). While the instant specification and the art provide methods for finding other *yjgF* ORFs in *Escherichia* whose inactivation may be useful for producing L-threonine or other L-amino acids, these methods do not enable one of skill in the art to make all, or a relevant portion of, the molecules within the scope of the claims. The ability to find a *yjgF* ORF within the scope of the instant claims is not equivalent to the ability to make and use a *yjgF* ORF as required by the statute (i.e., "make and use"). In addition, the nature of the invention is that no common function has been assigned for the family of *yjgF* ORF's (Volz *et al.*, Enos-Berlage *et al.*, see IDS). Thus, inactivating *yjgF* ORF's encompassed by the scope of the claims would be wholly unpredictable since the family is not disclosed as sharing a common function.

In addition, no working examples of using *Escherichia* in which the *yjgF* ORF is inactivated for producing L-amino acids other than L-threonine have been provided. The nature of the invention is such that L-threonine is a member of the oxaloacetate amino acid biosynthetic family, which is one of six amino acid biosynthetic pathways (Table 21-1 Lehninger *et al.*, see PTO-892); even amino acids within the same biosynthetic pathway have unique pathway steps (see pages 697-715, Lehninger *et al.*, see PTO-892). Hence, to use *Escherichia* in which a *yjgF* ORF has been inactivated for producing L-amino acids other than L-threonine would be wholly unpredictable. Inactivated *yjgF* could have the effect of inhibiting production of other L-amino acids. The list of genes in claims 17-18 to be expressed or inactivated are not all disclosed as being useful for the production of L-threonine. For example, while expressing *rhtC* is useful because it imparts threonine resistance, the effects of expressing *rhtB*, which imparts homoserine resistance, would be wholly unpredictable on the production of L-threonine. Expressing or

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inactivating particular genes in conjunction with an inactivated *yjgF* ORF could counter-act the affect of *yjgF* ORF as being useful in L-threonine production. The specification and the art provide no guidance on using many of the genes listed in claims 17-18 for producing the scope of L-amino acids claimed. While the art provides methods for finding conditions under which *Escherichia* in which particular genes are expressed or inactivated produce particular L-amino acids, these methods do not do not enable one of skill in the art to use all, or a relevant portion of, the *Escherichia* within the scope of the claims. The ability to find conditions under which an *Escherichia* bacterium with particular genes are expressed or inactivated produces a given amino acid is not equivalent to the ability to use the instant *Escherichia* as required by the statute (i.e., “make and use”).

In conclusion, to make and use all the *Escherichia* or *Escherichia coli* in which *yjgF* ORF is inactivated (claims 11, 14-27) and in which particular genes are additionally expressed or inactivated (claims 17-18) for producing all the L-amino acids (claims 11-14, 16-27) included in the breadth of the claims would require undue experimentation. Therefore, the instant claims are not enabled to the full extent of their scope.

Other Art for Comment/Examiner's Suggestions

The following are cited to complete the record:

- a) Enos-Berlage (see IDS) teach that the attenuation of *S. typhimurium yjgF* causes a defect in isoleucine biosynthesis. Using inactivated *yjgF* and recovering/isolating L-amino acids is not taught or indicated.

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- b) WO 02/36797 (Degussa *et al.*, see IDS) teaches attenuation of *poxB* for fermentative preparation of L-amino acids, in particular L-threonine. Using *yjgF* is not taught.
- c) Volz *et al.* (see IDS) teach the atomic resolution structure of *E. coli yjgF* (SEQ ID NO: 1) and a functional analysis of the structure; however, they do not definitively identify a function, although they suggest a link to tyrosine phosphatases. The use of *yjgF* for producing amino acids is not suggested.
- d) Blattner *et al.* (see IDS) teach SEQ ID NO: 1, but they do not teach a function for SEQ ID NO: 1 or its inactivation in a method to isolate L-amino acids.

Conclusion

18. Claims 11-27 are rejected for the reasons identified in the numbered sections of the Office action. Applicants must respond to the objections/rejections in each of the numbered sections in the Office action to be fully responsive in prosecution.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lindsay Odell whose telephone number is 571-272-3445. The examiner can normally be reached on M-F, 8:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lindsay Odell, Ph.D.
June 28, 2005


KATHLEEN KERR, PH.D.
PRIMARY EXAMINER
SPE